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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/809,291	03/25/2004	Cynthia C. Bamdad	M1015.70002US01	6035

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EXAMINER	
COUNTS, GARY W	
ART UNIT	PAPER NUMBER
1641	

NOTIFICATION DATE	DELIVERY MODE
08/16/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

uspto@jhkiplaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/809,291	BAMDAD ET AL.	
	Examiner	Art Unit	
	GARY W. COUNTS	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *217,218,220,221,223-227,229-235,237,238,240 and 241* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *217, 218, 220, 221, 223-227, 229-235, 237, 238, 240 and 241* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

The amendment filed 05/24/10 is acknowledged and has been entered. Currently, claims 217, 218, 220, 221, 223-227, 229-235, 237, 238, 240 and 241 are pending and under examination.

Withdrawn Rejections

All rejections of claims not reiterated herein, have been withdrawn.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 217, 218, 223, 225-227, 230, 231, 233-235 and 240 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bamdad et al (US 6,541,617) in view of Charych et al (US 6,001,556).

Bamdad et al disclose method for immobilizing a colloid particle to a non-colloidal structure. Bamdad et al disclose a transport particle (5) comprising a linker (60) and a binding ligand (55) (e.g. Fig 1C, col 2 - col 3). Bamdad et al disclose that the transport particle can be colloidal (col 37). Bamdad et al disclose an electrode (non-colloidal structure (85) comprising a linker (60) and a binding ligand (65) (e.g. Fig 1C). Bamdad et al disclose the ligand (65) of the non-colloidal structure binds to the ligand (55) of the colloidal transport particle to immobilize the colloidal particle to the non-colloidal structure. Bamdad et al disclose that the colloidal transport particle can comprise a fluorescent label (signaling entity) (col 41). Bamdad et al discloses the detection complexes comprising the colloidal particle bound to the non-colloidal structure. Bamdad et al disclose the particle can comprise self-assembled monolayers (SAM) (e.g. col 2) (It is noted that in the Remarks section of the amendment filed 12/13/07 applicant directed Examiner's attention to paragraph 91 in the patent application

publication number US 2005/0148101 for support for the term "non-adsorbent surface", a review of which indicates that SAM's resist nonspecific adsorption without protein blocking steps). Thus, Bamdad teaches a non-adsorbent surface. Bamdad et al also discloses that the electrode can comprise SAM's (e.g. col 9-10 and that the electrodes can be chips)(e.g. col 10).

Bamdad et al differ from the instant invention in failing to teach allowing the colloidal particle the ability to fasten to the non-colloidal structure in the presence of a candidate drug for interruption of the binding of the ligand.

Charych et al disclose a competitive assay in which a drug candidate is introduced into a system containing a receptor and its reciprocal binding partner. Charych et al disclose that if the drug binds to the receptor or modifies the binding partner's binding capacity, there is a decrease in the signal (col 20, lines 1-40). Charych et al disclose that this provides for the development and improvement of drugs by observing competitive inhibition of natural binding events between all surfaces or binding sites and their natural bioactive ligand.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate candidate drugs and incorporate receptors (ligand) and reciprocal binding partners (target) as taught by Charych et al into the method of Bamdad et al because Charych et al shows that this provides for the development and improvement of drugs by observing competitive inhibition of natural binding events between all surfaces or binding sites and their natural bioactive ligand. Also, with respect to the recitation "allowing the colloidal particle the ability to fasten to the non-

colloidal structure in the presence of a candidate drug". Since Bamdad et al provides the same binding partners as currently recited, the binding partner of Bamdad et al would have the ability to fasten to the non-colloidal structure in the presence of a candidate drug.

Further, the recitation "for interruption of binding of the ligand to a target" is a recitation of intended use and does not provide any positive active method steps. The examiner notes that such statements are directed to the intended use of the claimed invention. Applicant is reminded that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art. If the prior art is capable of performing the intended use then it meets the claim. In the instant case, Bamdad et al teaches the same components and structures as currently recited and thus would have the ability to fasten to the non-colloidal structure in the presence of a candidate drug. Nevertheless, as shown above it would have been obvious to one of ordinary skill in the art to incorporate candidate drugs and receptors and reciprocal binding partners as taught by Charych et al into the method of Bamdad et al because Charych et al shows that that this provides for the development and improvement of drugs by observing competitive inhibition of natural binding events between all surfaces or binding sites and their natural bioactive ligand. Thus, for the reasons stated above the combination of Bamdad et al and Charych et al reads on the instantly recited claims.

5. Claims 220, 229 and 237 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bamdad et al in view of Charych et al as applied to claims 217, 218, 223, 225-228, 230, 231, 233-235 and 240 above, and further in view of Altieri et al (US 6,346,389).

See above for the teachings of Bamdad et al and Charych et al.

Bamdad et al and Charych et al differ from the instant invention in failing to teach the binding partner is adapted for linkage to the particle by glutathione/glutathione-s-transferase ligand interaction.

Altieri et al disclose glutathione-s-transferase fusion proteins which are immobilized onto a glutathione substrate. Altieri et al disclose that this immobilization allows for the separation of protein-protein complexes from uncomplexed forms, as well as to accommodate automation of an assay (col 10, lines 9-36).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate glutathione-s-transferase fusion proteins and glutathione substrates as taught by Altieri et al into the modified method of Bamdad et al because Altieri et al teaches that this immobilization allows for the separation of protein-protein complexes from uncomplexed forms, as well as to accommodate automation of an assay.

6. Claim 221 and 238 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bamdad et al in view of Charych et al as applied to claims 217, 218, 223, 225-228,

230, 231, 233-235 and 240 above, and further in view of Zeytinoglu et al (US 6,080,539).

See above for the teachings of Bamdad et al and Charych et al.

Bamdad et al and Charych et al differ from the instant invention in failing to teach the non-colloidal structure is a cell or tissue section.

Zeytinoglu teaches a method of detecting antigens in which an antibody is brought into contact with the body component in situ, and the resulting antibody/antigen complex is then detected either in situ or ex situ (col 2, lines 65 – col 3, line 2). A retainer is applied to a body part such as the skin or mucous membrane of a patient, and one or more fist step antibodies are brought into contact with the body part within the confines of the retainer. Antibody/antigen complex is then amplified to an appropriate level, and a second step antibody is brought into contact with the complex to render the complex macroscopically detectable (col 3, lines 3-12).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to detect antigens in situ on cell or body tissue as taught by Zeytinoglu using the modified method and reagents of Bamdad et al because both teach using colloidal particles as a signal label for detecting a target analyte. One of ordinary skill would combine these references so that antigen on cells and or body tissue can be detected directly without taking biopsies and using biotin/streptavidin to amplify signal or to secure the binding of the antibody or the label to the complex being detected.

7. Claim 224, 232, and 241 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bamdad et al in view Charych et al as applied to claims 217, 218, 223, 225-228, 230, 231, 233-235 and 240 above, and further of Virtanen et al (US 6,342,349).

See above for the teachings of Bamdad et al and Charych et al.

Bamdad et al and Charych et al differs from the instant invention in failing to teach exposing the colloid particle and the non-colloidal structure to a substrate for an enzyme adapted for linkage to the non-colloidal structure, a molecule species linkable to the substrate via enzyme activity adapted for linkage to the particle, and an enzyme for the substrate.

Virtanen et al disclose an immunoassay method comprising colloid particles (col 37, lines 40-42), which are immobilized to a substrate (non-colloidal structure). Virtanen et al disclose that the colloid particle and the substrate (non-colloidal structure) are exposed to cleavable spacer molecules (entity), which comprise cleavage sites. (see figures 1 and 3). Virtanen et al disclose that the cleavable spacer molecules bind to both the colloid particle and to the non-colloidal structure. Virtanen et al disclose that enzymes can be used as cleavage reagents by incorporating into the spacer a moiety that serves as the substrate (enzyme substrate) for the given enzyme (col 34, lines 15-17). Virtanen et al disclose that the analyte can be a drug candidate (col 55, line 53 – col 56, line 67). Virtanen et al disclose that the cleavable spacer molecules also comprise antibodies specific for the analyte of interest. Virtanen et al disclose that when the analyte (drug candidate) is present it binds to the antibody and prevents the

chemical cleaving agent (enzyme) from cleaving the colloid particle from the surface (col 18, lines 1-16). Virtanen et al disclose that the presence and absence of the colloid particle may then be detected. Virtanen et al teaches that such cleavable signal embodiments provide advantages for immunoassays and provides for both fast and sensitive detection (col 19).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate substrates, enzymes and molecular species such as taught by Virtanen et al into the modified method of Bamdad et al because Virtanen et al teaches that it is known in the art to use such reagents for determining the bound state of non-colloidal structure to a colloidal particle and also teaches that such embodiments provides advantages for immunoassays and provides for both fast and sensitive detection (col 19).

Response to Arguments

8. Applicant's arguments filed 05/24/10 have been fully considered but they are not persuasive.

Applicant argues that Charych fails to disclose or suggest drug screening in a competitive assay compared with the methods of the claimed invention. Applicant states that Charych discloses using a lipid bilayer which is impregnated with a dye that signals one way when the bilayer is unperturbed but then, if a binding partner binds to it causing the bi-layer to be perturbed, thin its signal changes. Applicant states that therefore, there are at least two differences between Charych and the claimed invention. Applicant states that first the Charych method looks for interruption of binding

before the interaction between the binding partner on the colloid and its ligand on the surface occurs and that second the binding partner in the method of Charych's method simply cannot be attached to the non-colloidal surface.

These arguments are not found persuasive because it appears that Applicant is arguing the references individually. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Further, with respect to the interruption of binding as argued by the Applicant. As stated above the Examiner has relied upon incorporating receptor/ligand interactions and drug candidates and competition into the methods of Bamdad et al and with respect to the limitation "allowing the colloidal particle the ability to fasten to the non-colloidal structure in the presence of a candidate drug", Bamdad et al specifically teaches that ligand/receptors can be used in the methods (col 27, lines 35-37) and thus the modified method of Bamdad et al would have the same binding partners as currently recited, the binding partner of Bamdad et al would have the ability to fasten to the non-colloidal structure in the presence of a candidate drug. Also, the recitation "for interruption of binding of the ligand to a target" is a recitation of intended use and does not provide any positive active method steps. The examiner notes that such statements are directed to the intended use of the claimed invention. Applicant is reminded that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art. If the prior art is

capable of performing the intended use then it meets the claim. Thus, if Applicant intends that the ligand and receptor are bound even in the presence of the drug candidate and that the candidate drug does not interrupt this binding, then Applicant should positively recite such limitations in the claims.

Applicant argues that Charych discloses a method for screening for a drug by somehow preventing known binding of a receptor and a target and that once the binding has occurred, the Charych method does not allow for any competitive binding away of the receptor. Applicant states that in contrast, the inventive assay uses a candidate drug that disrupts or competes away the ligand and competes away the signal even after the binding between the ligand and its binding protein has occurred.
This argument is not found persuasive because 1) of reasons stated supra concerning the recitations "allowing the colloidal particle the ability to fasten to the non-colloidal structure in the presence of a candidate drug for interruption of binding of the ligand to the target binding partner" and 2) the limitations "a candidate drug that disrupts or competes away the ligand and competes away the signal even after the binding between the ligand and its binding protein has occurred" are not recited in the current claims. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a candidate drug that disrupts or competes away the ligand and competes away the signal even after the binding between the ligand and its binding protein has occurred) are not recited in the rejected claim(s). Although the claims are interpreted in

light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant further argues that even if the references were to be hypothetically combinable, neither reference provides any motivation to combine the references to arrive at the claimed invention.

This argument is not found persuasive because as stated in the previous office action and above Charych et al specifically teaches that the use of receptor/ligand interactions and candidate drugs in competition assays provides for the development and improvement of drugs by observing competitive inhibition of natural binding events between all surfaces or binding sites and their natural bioactive ligand. Further, as stated above Bamdad et al specifically teaches that receptor/ligand interactions can be used in the assays and thus absent evidence to the contrary, one of ordinary skill in the art would have a reasonable expectation of success incorporating receptors and ligands on the colloidal and non-colloidal structures of Bamdad et al and using the structures in assays incorporating candidate drugs.

Applicant argues that even if the references were combined the results is not a competitive binding assay as in the claimed invention.

This argument is not found persuasive because of reasons stated above that the combined references of Bamdad et al and Charych et al teach the same structures and method steps which are positively recited. Thus, the rejections are maintained.

Applicant's remaining arguments directed to the references of Altieri, Zeytinoglu and Virtanen appear to argue that these reference fail to cure the deficiencies of Bamdad et al and Charych et al.

These arguments are not found persuasive because of reasons stated above that the combination of Bamdad et al and Charych et al read on the instantly recited claims. Therefore, the combinations with Altieri, Zeytinoglu and Virtanen are maintained.

Conclusion

9. No claims are allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GARY W. COUNTS whose telephone number is (571)272-0817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ Gary W. Counts/
Examiner, Art Unit 1641

/Melanie Yu/
Primary Examiner, Art Unit 1641